Hypersplenic Anæmia relieved by Splenectomy

By M. G. NELSON, M.D., M.R.C.P., M.R.C.P.(I)., D.T.M. & H.

Clinical Pathologist, Royal Victoria Hospital, Belfast

CONSIDERABLE interest has recently been aroused in the group of conditions characterised by anæmia, granulocytopenia and thrombocytopenia occurring alone or in association and accompanied by splenomegaly and a hyperplastic marrow. The triad of cytopenia, splenomegaly and hyperplastic marrow constitutes what might be called the 'hypersplenic syndrome.' This triad may be found in a number of diverse disorders in which splenomegaly is a constant finding. It has been noted in chronic infections such as syphilis, malaria, kala azar, brucellosis and Felty's syndrome; in portal hypertension and Banti's syndrome, and in lipoidal infiltrations, such as Gaucher's disease.

The evidence throughout this group seemed to point to the basic effect produced in the blood by the enlarged spleen, but lack of complete knowledge of the physiological functions of this organ has prevented full understanding of the pathogenesis. There are two possible hypotheses to explain the observed phenomena, and these have given rise to two schools of thought which might be broadly termed the "Hormonal" and the "Phagocytic." The former conception is that a pathologically hypertrophied spleen due to any cause produces a hormone which acts on the bone marrow, and depresses the maturation or release of the primitive cells of the erythrocytic, granulocytic and thrombocytic series. This hormone is considered to be elaborated by the reticulo endothelial cells of the spleen and its effect may be general, producing a pancytopenia or, selective producing a granulocytopenia, thrombocytopenia or anæmia. This theory has many supporters, particularly Naegeli, who applied the term 'hypersplenism' to the syndrome, and in this he has been ably supported by Dameskek (1947). The second theory envisages an increased phagocytic activity of the spleen produced by reticulo endothelial hypertrophy due to any cause. The reticulo endothelial cells engulf and destroy the blood cells more rapidly than they can be replaced by the marrow. Histopathological evidence of increased phagocytic activity has been adduced by Wiseman and Doan (1942).

Although cases of this type are uncommon, yet the satisfactory response which results from splenectomy in these cases prompted me to put on record this case of intractable macrocytic anæmia associated with a progressive splenomegaly, which had an excellent clinical and hæmatological response to splenectomy.

The patient, M. K., an unmarried woman of 54 years of age, was first seen in the medical out-patient department of the Royal Victoria Hospital on 11th August, 1948, because of loss of energy, breathlessness, palpitation and swelling of the ankles. These symptons were of gradual onset, had been present for a year, and had become progressively more noticeable. She also complained of a constant

pain in the right side of her abdomen which had been present for about one month, and this was associated with loss of appetite. The only relevant findings in the past history of this patient was that she had received injections in the United States of America in 1920 for a 'blood condition.' She did not know the nature of the 'blood condition,' but thought that the injections were arsenic, and closer enquiry revealed that the spacing and courses of these injections resembled those of anti-syphilitic arsenotherapy.

On examination, the patient was grossly anæmic but not jaundiced. She was small in stature and of a sallow complexion with pitting œdema of the lower limbs. There were no enlarged superficial lymph-glands. The nails were ridged and flattened and the tongue was smooth and moist. The skin exhibited a maculopapular rash with numerous scattered lesions which were most marked on the trunk. In colour, these spots varied from lilac to brown and in size, from a lentil to a sixpence. Some were raised and a few formed definite soft, sessile tumours soft to the touch and pigmented on top. The appearance of the tumours was suggestive of a diagnosis of von Recklinghausen's neurofibromatosis, and this was confirmed clinically by the dermatologists. On physical examination, the liver and spleen were both found to be grossly enlarged and palpable, but nothing abnormal was found on examination of the other bodily systems. Because of her history, the patient was seen in the venereal diseases department, where it was considered that the nature and distribution of some depressed scars on her back were consistent with a clinical diagnosis of syphilis, and serological tests for syphilis appeared to confirm this, as the Kahn reaction was doubtful, and the Wassermann positive.

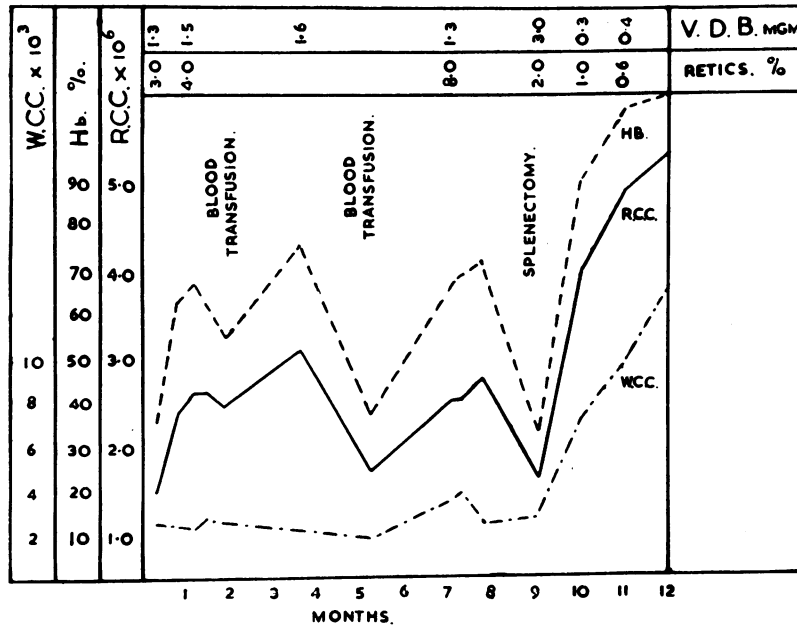
The initial examination of the peripheral blood revealed a gross anæmia (hæmoglobin = 36 per cent. Haldane = 5.1 g./100 ml., R.C.C. = 1,410,000/c.mm.); macrocytosis (M.C.V. = 94 c.μ.); leukopenia (W.C.C. = 2,500/c.mm.); hyperbilirubinæmia (Van-den-Bergh = 1.25 mg/100 ml.); a reticulocyte count of 3 per cent. The peripheral blood smear showed macrocytosis, anisocytosis and polychromasia, but no primitive red cells were seen. These findings were suggestive of a diagnosis of Addisonian pernicious anæmia, but a fractional test-meal revealed the presence of free acid in the stomach. This, together with the fact that the initial blood examination showed 3 per cent. reticulocytes, was considered to weigh heavily against the diagnosis of pernicious anæmia. Unfortunately, a bone-marrow biopsy to determine the presence of megaloblastic hyperplasia was not carried out prior to treatment.

A diagnosis of aplastic anæmia (toxic pancytopenia), resulting from arsenotherapy, was considered unlikely because of the twenty-eight year interval since the last arsenic injection, but the possibility that the anæmia was of syphilitic origin was explored by testing the response of the anæmia to a therapeutic trial of anti-syphilitic drugs. Accordingly, the patient was given three intramuscular injections of 0.1 grams of bismuth and a course of penicillin consisting of six mega units spread over ten days. This therapy produced no hæmatological improvement.

The patient then received an adequate course of parenteral liver therapy combined with oral iron, and on this therapy the hæmoglobin rose from 36 per cent. to 63 per cent. in 14 days but this was associated with a constant reticulocytosis without any significant crisis. This response was satisfactory, but the absence of a reticulocytosis was unusual and the therapy complicated by combined oral iron and parenteral liver. Because macrocytic anæmias with free acid in the stomach usually respond more satisfactorily to oral folic acid than parenteral liver, a course of 15 mg. of oral folic acid daily was given for fifteen days without any further hæmatological improvement. When on this treatment a bone marrow biopsy was carried out which showed a markedly hyperplastic marrow due to normoblastic proliferation and megaloblasts were not seen.

The patient was discharged from hospital on weekly injections of liver extract and daily oral iron. She was seen from time to time as an out-patient between November, 1948, and June, 1949, when it was noted that the splenomegaly was increasing and the hæmoglobin, despite adequate therapy, was not being maintained, so that, on two occasions, blood transfusions were required. Thus, this patient was under observation for some eleven months, during which time she was on hæmatinic therapy without significant benefit. Although the anæmia in this case was consistently macrocytic, the evidence for the diagnosis of Addisonian pernicious anæmia was incomplete, viz., presence of free acid in the stomach, inability of liver therapy to maintain the blood level.

Following an attack of herpes zoster in April, 1949, she was re-admitted into the Royal Victoria Hospital in June of the same year. When the hæmatological records of this patient were reviewed, it was seen that she had a persistent anæmia



not maintained by hæmatinic therapy, a hyperplastic marrow, splenomegaly, hyperbilirubinæmia, and a constant reticulocytosis. These findings were suggestive of a hæmolytic anæmia. That this hæmolytic anæmia was of mild degree and unlike either congenital or acquired hæmolytic anæmia, was evident by the mild degree of the reticulocytosis; by the absence of crisis, by the absence of spherocytosis; by the normal osmotic fragility of the red cells, and by the repeatedly negative Coomb's test (anti-human globulin test). It was considered that hypersplenic anæmia seemed to be the most probable diagnosis, and accordingly, following pre-operative preparation by the transfusion of four pints of compatible blood, a splenectomy was performed. The hæmoglobin, eight days after the splenectomy, was 90 per cent., and this level has been maintained and improved since then. This improvement has been associated with a rise in the red cell and white cell counts; a normal bilirubin level in the blood; and a normal reticulocyte count.

The spleen, when examined after removal, was greatly enlarged and weighed 1,500 gm. The histological pattern of the spleen was well preserved. There was a general increase in the cellularity of the pulp with thickening of the sinusoidal walls. This increased cellularity was in part due to a proliferation of reticulum cells of the pulp and also of the lining cells of the splenic sinusoids which were unduly prominent. Follicular aggregations of reticulum cells without giant cell formation were evident, both in the lymph follicles and in the perifollicular zone. These resembled similar lesions found in the spleen in Brucella abortus infection, but in this case the agglutination test for brucellosis was negative. The lymph follicles throughout the spleen were rather small. Hæmosiderosis was marked throughout the pulp, but erythrophagocytosis was not conspicuous.

Comment

The hæmatological findings and response to splenectomy in this case satisfy the criteriæ laid down by Doan (1946) for splenic blood dyscrasia or hypersplenic anæmia, namely :—

1. Diminution of one or more of the circulating elements of the blood.
2. Normal or increased bone marrow activity.
3. Splenic enlargement.
4. Complete, rapid, clinical and hæmatological recovery following splenectomy.

The histological findings in the spleen after removal were those of a diffuse hyperplasia of the reticulum cells, with nodular 'pseudofollicles' of reticulum cells in relation to the lymph follicles, and there was no histological evidence of syphilitic involvement of the spleen. These findings are similar to those described by Haam & Awny (1948) in ten cases of splenic panhæmatocytopenia.

The relationship of syphilis to the clinical condition in this case, if any, is difficult to evaluate. This is further complicated by the results of the serological tests for syphilis before and after splenectomy.

		Kahn		W/R.	
26/ 8/1948	...	+2	...	++	
6/ 1/1949	...	+1	...	++	
21/ 3/1949	...	+2	...	++	
1/ 6/1949	...	+1	...	++	Splenectomy
7/ 7/1949	...	—	...	—	
3/ 8/1950	...	—	...	—	
5/10/1950	...	—	...	—	

It is possible that the positive results found with the serological tests for syphilis may have been false, and associated with the hæmolytic anæmia found in the hypersplenic syndrome. Information on this point, in the literature, is lacking, but false positive Wassermann results have been reported in hæmolytic anæmia by Rubenstein (1948). In this department, of eighteen cases of hæmolytic anæmia, where syphilis was excluded, false positive W/R results were found in three, doubtful results in two, and negative in the remainder. Our own findings have tended to suggest that these false serological results are associated mainly with periods of crisis which did not occur in this case. However, the coincidental reversal of the positive serology to negative associated with the removal of evidence of active hæmolysis following splenectomy suggests a possible relationship between these findings.

Summary

A case of hypersplenic anæmia with panhæmatocytopenia, splenomegaly and hyperplastic marrow, showing an excellent response to splenectomy is described.

References.

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REVIEW

BRONCHIOGENIC CARCINOMA AND ADENOMA. With a Chapter on Mediastinal Tumours. By B. M. Fried, M.D.

An extremely well produced book, with only a few typographical errors. The reproductions of X-ray film and microphotographs are particularly good; an extensive, bibliography is given at the end of each section. Every aspect of carcinoma is meticulously discussed, the chapters on pathology, metastases, and the combination of carcinoma and tuberculosis being very good.

Bronchiogenic adenoma is very well done. The comparison to an iceberg, as regards the endo-bronchial and extra-bronchial portions, is very apt, with reference to endo-bronchial methods of dealing with the tumour.

Doctor Fried is a physician, and so does not discuss details of surgical treatment. He gives the accepted contraindications. Regarding treatment by radiation, there is some evidence nowadays that the results may be somewhat better than he has indicated.

A book to be recommended. G. R. B. P.